the LA during atrial contraction followed by rapid LAA filling in systole; less rapid LAA emptying during early diastolic LV filling; oscillatory LAA flow in mid-diastole as LA and LV pressures crossover. We simulated three clinical states: normal LAA contraction, inactive LAA ("stunned" LAA after cardioversion from fibrillation to sinus rhythm), and no LAA at all. We calculated cardiac index (CI, l/min/m^2), early-diastolic and late-diastolic ME (MF-E and MF-A, ml/s), and mean LAP (mmHg). Loss of LAA contraction reduces MF-A and increases MF-E by elevating LAP. Of note, the inactive LAA produces the least efficient atrioventricular blood transfer with lowest CI and highest mean LAP – less efficient hemodynamics than either a normal LAA or no LAA at all. Thus, a properly-timed left atrial appendage contraction improves left ventricular filling dynamics and minimizes left atrial pressure.

	CI	MF-E	MF-A	MLAP
Normal LAA	1.30	54	90	2.5
Inactive LAA	1.23	104	66	3.3
Absent LAA	1.34	49	94	2.4

1015-134 Assessment of Left Atrial Pressure-Volume Relation Using Retrograde Left Atrial Catheterization and Echocardiographic Automatic Boundary Detection

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In the traditional separation of left atrial (LA) function reservoir, conduit and pump functions are included. A method such as pressure-volume (p-v) analysis that integrates data from the entire cardiac cycle can evaluate LA performance in physiologic investigation. We have applied real-time two-dimensional echocardiographic imaging with automatic boundary detection (ABD) to the accurately estimation of LA volume changes simultaneously with a Millar's catheter-tip micromanometer introduced retrogradely into the LA via the mitral valve to obtain the LA pressure, using a steerable cardiac catheter. Six normal subjects during atrial pacing at heart rate levels equal to those expected after dobutamine administration, were studied. LA end diastolic volume (V_a) was measured at the volume immediately preceding atrial shortening following the P wave of the electrocardiogram. The LA p-v relation was composed of two loops: the A loop, expressing the pump function of the left atrium and the V loop, expressing the reservoir function of the LA. Pressure and volume data during the ascending limb of the V loop were fitted to the exponential function, $P = bxe^{a.V}$, where P = pressure, V = volume, a was the passive elastic chamber stiffness constant (mm^{-1}) and b was the elastic constant (mmHg). A significant increase in area of A loop (from 163 to 288 ml.mmHg, $p < 0.001$) and in area of V loop (from 42 to 254 ml.mmHg, $p < 0.001$) was found. The difference between the area of A loop and the area of V loop (net atrial work) expressing the energy added by the LA to its contents significantly decreased from 121 to 34 ml.mmHg, $p < 0.001$. Furthermore, there was an improvement of LA diastolic function as the diastolic p-v plot was displaced downward and the a decreased (from 0.0166 to 0.0035 mm^{-1}, $p < 0.001$). *Conclusion:* In normal hearts LA pump function and LA distensibility may acutely increase with inotropics while LA contribution to left ventricular filling may acutely decrease by means of myocardial function improvement.

TUESDAY POSTER

1016 Calcium Mediated Contraction in Heart Failure

Tuesday, March 18, 1997, 3:00 p.m.–5:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: 3:00 p.m.–4:00 p.m.

1016-149 Calcium Transport Is Impaired in Sarcoplasmic Reticulum of Failed Human Hearts Due to Ischemic Cardiomyopathy Compared to Idiopathic Dilated Cardiomyopathy

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Recent studies have shown that sarcoplasmic reticulum (SR) Ca^{2+} transport is unchanged in human idiopathic dilated cardiomyopathic (IDC) hearts compared to normal hearts. We compared SR Ca^{2+} release channel density and Ca^{2+} ATPase activity and protein level in LV tissue of explanted failed human hearts due to IDC (n = 6) and to ischemic cardiomyopathy (ICM, n = 6). The density (Bmax) and affinity (Kd) of SR Ca^{2+} release channels were determined using [^{3}H]ryonadine binding. Thapsigargin-sensitive Ca^{2+} ATPase activity (μmol Pi released/min/mg protein) and tissue protein level were determined in isolated SR fraction. Ca^{2+} ATPase protein level was quantified in densitometric units/5 μg protein.

	IDC	ICM
Bmax (fmol/mg protein)	1212 ± 32	859 ± 54*
Kd (nM)	1.5 ± 0.2	1.2 ± 0.3
Ca^{2+} ATPase activity	0.15 ± 0.01	0.11 ± 0.01*
Ca^{2+} ATPase (protein)	2.6 ± 0.4	0.8 ± 0.3*

*P < 0.05 IDC vs. ICM

The results indicate that Bmax of SR Ca^{2+} release channels is reduced in ICM compared to IDC without changes in Kd. Ca^{2+} ATPase activity and protein level are also lower in ICM compared to IDC. *Conclusions:* In failed explanted human hearts, SR Ca^{2+} transport is impaired in ICM compared to IDC. The presence of abnormalities of cardiac SR Ca^{2+} transport in heart failure may depend on the etiology of the disease.

1016-150 Abnormal Intracellular Calcium Response to Increased Frequency of Stimulation in Failing Human Hearts

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Human heart failure is characterized by abnormal intracellular calcium handling, decreased sarcoplasmic reticulum Ca^{2+}-ATPase activity and an abnormal force-frequency relationship. To assess whether abnormal intracellular Ca^{2+} mobilization ($[Ca^{2+}]_i$) release or uptake by the SR contributes to the negative force-frequency relationship in failing human hearts, we evaluated the frequency response of $[Ca^{2+}]_i$, measured with the bioluminescent protein aequorin, in electrically driven trabeculae from the left ventricles of 6 failing (F) and 5 non-failing (NF) human hearts at 37ºC. In NF trabeculae, increasing frequency of stimulation from 0.1 to 2.0 Hz increased the force of contraction (FOC) (% Δ = 98 ± 11%) and peak $[Ca^{2+}]_i$ (1.3 ± 0.1 to 1.8 ± 0.2 μmol/l) while shortening the relaxation phase of the $[Ca^{2+}]_i$ transient ($L_{80\%}$: time to 80% relaxation of the $[Ca^{2+}]_i$ signal: 116 ± 13 to 92 ± 9 msec). In F trabeculae increasing frequency of stimulation from 0.1 to 1.0 Hz increased the FOC (% Δ = 67 ± 13%) and peak $[Ca^{2+}]_i$ (1.2 ± 0.1 to 1.7 ± 0.2 μmol/l) while $L_{80\%}$ remained unchanged (167 ± 14 to 183 ± 18 msec). Further increases of the stimulation frequency from 1.0 to 2.0 Hz decreased the FOC (% Δ = −58 ± 9%) and peak $[Ca^{2+}]_i$ (1.7 ± 0.2 to 0.6 ± 0.2 μmol/l) while significantly prolonging $L_{80\%}$ (183 ± 18 to 274 ± 21 msec). We conclude that 1) abnormal intracellular calcium contributes to the abnormal force-frequency relationship observed in F hearts, and 2) depressed SR Ca^{2+} ATPase activity in F myocardium leads to abnormal Ca^{2+} uptake and loading of the SR at high frequencies of stimulation

1016-151 Downregulation of the Calcium-binding Protein S100 A1 in Human Cardiomyopathy as Detected by HPLC and Electrospray-Ionisation-Mass-Spectrometry (ESI-MS)

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Introduction: The calcium-binding protein S100A1 has been shown to stimulate the Ca^{2+}-induced Ca^{2+}-release. Since an altered regulation of the SR Ca^{2+}-release-channel might account for a decreased Ca^{2+}-release observed in human end stage heart failure, we hypothesized that a change in S100A1 gene-expression might correlate with this finding. *Methods:* Left ventricular tissue from patients with end stage heart failure was investigated (coronary heart disease: n = 6; dilative cardiomyopathy: n = 6) and compared to control specimen (n = 3) deriving from donor hearts. After EDTA-extraction Ca^{2+}-binding proteins (CaBP) were prepurified by octylsepharose chromatography and finally fractionated by reverse-phase HPLC (RP 300, C8). The eluting CaBP were identified by ESI-MS and S100A1 quantified by a peak integrator. *Results:* While ESI-MS analyses revealed identical molecular masses for S100A1 in failing hearts and controls (10460Da), integration of eluting S100A1 peaks documented a significantly lower protein concentration in all myopathic samples yielding two groups with either < 75% (69 ± 6%) or < 35% (23 ± 12%) as compared to controls (100 ± 8%, $p < 0.001$). No correlation was seen with the underlying disease. *Conclusion:* In human cardiomyopathy S100A1 protein levels are significantly downregulated, while unchanged molecular masses exclude a differential posttranslational pro-